REMARKS

Applicants respectfully request reconsideration of the present application.

CLAIMS STATUS

Pending claims include rejected claims 32-33 and 35 and withdrawn claims 1-31, 34 and 36-37.

AMENDMENT TO THE SPECIFICATION

Applicants have amended the first paragraph of the specification and deleted the last paragraph presented on the amended page 32 to claim the benefit of US provisional applications nos. 60/148,101 and 60/198,621. No new matter has been added.

REJECTION UNDER 35 U.S.C. § 103(a)

Claims 32-33 and 35 stand rejected as obvious over Jacob et al. (WO99/24401), in view of Platt et al. (US patent No. 5,580,884) and Defoin et al. (Tetrahedron, 1997, vol. 53(40), p. 13783-17396) and further in view of van den Broek et al. (Recl. Trav. Chim Pays-bas, 1994, vol. 113, pp. 507-516). Applicants respectfully traverse.

Applicants organize the response in the following four parts:

1) Applicants' interpretation of the prior art references cited in the Office Action;

2) The PTO's formulation of the rejection;

3) Applicants' interpretation of the rejection;

4) Applicants' rebuttal of the rejection based on the PTO's failure to establish *prima facie* obviousness.

1. PRIOR ART REFERNCES

Jacob teaches *N*-substituted-1,5-dideoxy-1,5-imino-D-glucitol or galactitol compounds, see e.g. page 14, lines 3-8. Jacobs further teaches that *N*-substituent R can be C_1 to C_{20} alkyl, containing 1 to 5, preferably 1 to 3, most preferably 1 to 2, oxygen atoms, see page 15, lines 7-10.

Jacob, however, does not disclose any N-substituted 1,5,6-trideoxy-1,5-imino-D-galactitol compounds, including N-alkylated 1-methyl-deoxygalactonojirimycin (MeDGJ) compounds or an oxa substited derivative thereof as recited in the rejected claim 32. The PTO admits this deficiency of Jacob by stating that "Jacob et al. does not teach N-nonyl-1,5,6-trideoxy-1,5-imino-D-galactitol nor N-(7-oxa-nonyl)-1,5,6-trideoxy-1,5-imino-D-galactitol compounds", see Office Action, page 4, 2nd paragraph.

Platt teaches N-alkyl dervatives of deoxygalactonojirimycin (DGJ), in which the alkyl contains from 3-6 carbon atoms, see column 1, lines 36—40. Platt further teaches that these C3-C6 N-alkyl DGJ derivatives "can be used at concentrations of about 10-fold less than the effective antiviral concentrations of the corresponding N-alkyl derivatives of DNJ", see Platt, column 1, lines 52-55. Applicants believe that the PTO uses this statement in Platt to support an assertion that "DGJ has been shown to have better inhibitory activity compared to N-alkyl-deoxynojirimycin (DNJ)", see Office Action, page 4, 3rd paragraph. Applicants respectfully submit that Platt's statement in column 1, lines 52-55, and the PTO's assertion conflict with Applicants' data summarized in Table 2 of the present application, which show that N-butyl DNJ has an antiviral effect on bovine virus diarrhea virus (BVDV) in Madin-Darby bovine kidney (MDBK), while N-butyl DGJ does not.

Summarizing, Platt teaches C3-C6 N-alkyl deoxynogalactitols. Platt teaches neither N-substituted 1,5,6-trideoxy-1,5-imino-D-galactitol compounds, including N-alkylated 1-methyl-deoxygalactonojirimycin (MeDGJ) compounds or an oxa substited derivative thereof as required by the pending claims, nor N-substituent, that is C_8-C_{16} alkyl or an oxa-derivative thereof, as also required by the pending claims. Furthermore, Platt does not remedy deficiencies of Jacob as Platt provides neither suggestion, nor motivation to modify Jacob's compounds into N-alkylated 1-methyl-deoxygalactonojirimycin (MeDGJ) compounds or an oxa substited derivative thereof.

Defoin teaches that true aminosugars are rather unstable compounds that can be easily reduced or oxidized to the corresponding 1-deoxy or δ-lactams, which possess similar inhibitory properties (with respect to the corresponding glycosidases) when compared with true amino-sugars, see page 13783. Defoin further teaches that compound D-3b, which is 1,5,6 trideoxy-D-galactitol, is known, see page 13786.

Van den Broek teaches synthesis of oxygen substituted N-alkyl 1-deoxynojirimycin derivatives. On page 508, van den Broek teaches that N-decyl-deoxynojirimycin is a potent α-glucosidase inhibitor in the HepG2 assay but showed significant toxicity. Van der Broek postulates that such toxicity is due to amphiphilic properties associated with the structure of N-decyl-deoxynojirimycin: a lipophilic side chain attached to a polar aza-sugar ring. According to van den Broek, this "amphiphilicity i.e., can be eliminated (1) either by decreasing the lipophilicity of the N-decyl side-chain or (2) increasing the lipophilicity of the aza-sugar. Earlier we showed that modification of the hydroxyl function (s) **is detrimental to the activity** of the compounds," see page 508, left column, third full paragraph.

2. PTO's FORMULATION OF THE REJECTION

The PTO formulates the obviousness rejection on pages 5-6 of the Office Action as follows:

1) "It would have been obvious to one of ordinary skill in the art to use the 1,5-dideoxy and 1,5,6-trideoxy alditols with D-galacto configuration of Platt et al. and DeFoin et al. in the Jacob et al. formula 1 compounds as the Jacob et al. compounds differ only in that they disclose only 1,5-dideoxy alditols."

2) "One would have been motivated to make such a change as van den Broek et al. demonstrate that changes in the aza-sugar portion of deoxynojirimycin that would increase its lipophilicity would alter the toxicity profiles of the compounds. Removal of a hydroxyl group at the 6-position would result in an increase in the lipophilicity of the aza-sugar."

3) "Further Platt et al. demonstrated that the deoxygalactojirimycin compounds demonstrate increased inhibition compared to deoxynojirimycin."

4) "One would expect reasonable chance of success as DeFoin et al. details the synthesis of the 1,5,6-trideoxy D-galactitol compounds and Jacob et al. and Platt et al. demonstrate the introduction of the alkyl moieties on the ring nitrogen."

5) "Further Jacob et al. details the synthesis of 1,5-dideoxy D-galactitol the process of which could easily be modified to utilize DeFoin et al. 1,5,6-trideoxy D-galactitol moieties."

3. APPLICANTS' UNDERSTANDING OF THE REJECTION

Applicants respectfully submit that statement 1 is vague and inaccurate for several reasons, one of which is that Platt does not teach 1,5,6-trideoxy alditols with D-galacto or any other configuration.

Nevertheless, as far as Applicants can understand, the PTO's intention in the rejection is to somehow combine Jacob's N-substituted-1,5-dideoxy-imino galactitol compounds, which unlike the claimed N-alkylated 1-methyl-deoxygalactonojirimycin (MeDGJ) or an oxa-substituted derivative thereof are not deoxy at the 6-position, i.e. Jacob's compounds have OH at the 6-position, while the claimed compounds do not, with Defoin's compound D3b, which has the same stereo-configuration as the claimed compounds and is deoxy at the 6-position like the claimed compounds, but lacks alkyl or oxa-alkyl N-substituents. In other words, the PTO believes it is obvious to modify Jacob's N-substituted-1,5-dideoxy-imino galactitol compounds by removing OH at the 6-position in view of Defoin. For a motivation for such a modification, the PTO relies on van den Broek, see the PTO's statement 2.

4. PTO FAILED TO ESTABLISH PRIMA FACIE OBVIOUSNESS AS VAN DEN BROEK TEACHES AWAY FROM MODYFYING HYDROXYL FUNCTION OF JACOB'S COMPOUNDS

Applicants respectfully submit that the PTO failed to establish a *prima facie* case of obviousness as one of ordinary would have neither a required motivation nor a required reasonable expectation of success to modify Jacob's N-substituted-1,5-dideoxy-imino galactitol compounds into the claimed N-alkylated 1-methyl-deoxygalactonojirimycin (MeDGJ) or an oxa-substituted derivative thereof by removing OH at the 6-position. Van den Broek, a reference on which the PTO relies for motivation for such a modification, in fact teaches away from performing the modification by stating "modification of the hydroxyl function(s) is **detrimental** to the activity of the compound." Thus, as no *prima facie* obviousness is established, Applicants request withdrawal of the rejection.

Applicants further submit that Platt cannot remedy the above deficiencies of the combination of Jacob, Defoin and van den Broek. For the record, Applicants submit that the PTO's statement 3 contradicts Applicants' experimental data, see discussion of Platt above.

Applicants do not address the PTO's statements 4 and 5 in the present response, however, Applicants reserve a right to present comments with respect to these statements if the PTO does not withdraw the rejection in view of the above commentary.

CONCLUSION

Applicants believe that the present application is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By _____

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